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NOTICE OF ALLOWANCE AND FEE(S) DUE

23117 7590 07/28/2009

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/28/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,336	12/01/2004	Philip John Birch	117-524	3696

TITLE OF INVENTION: FORMULATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	10/28/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23117 7590 07/28/2009

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

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EXAMINER	ART UNIT	CLASS-SUBCLASS
RAMACHANDRAN, UMAMAHESWARI	1617	514-282000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☐ Issue Fee

☐ Publication Fee (No small entity discount permitted)

☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/508,336	BIRCH ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *4/3/2009*.

2. ☒ The allowed claim(s) is/are *1-15, 38, 39, 41, 70-72, 74-77, 79 and renumbered as 1-26*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 7/14/2009
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview and email from Attorney Arthur Crawford on 7/09/2009, 7/16/2009. Claims 1, 70, 71, 72 and 74 will be amended. Claims 48-69, 73, 78 will be cancelled. Claims 1-15, 38, 39, 41, 70-72, 74-77, 79 are allowable and are renumbered as 1-26.

The application has been amended as follows:

1) In claim 1, line 5 after "nasal mucosa", **INSERT** **",** and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof"

2) **DELETE** claims 48-69, 73, 78

3) In claim 70, line 6, after "buprenorphine or" **INSERT** "physiologically acceptable"

4) In claim 70, line 8, after "2 hours" **INSERT** **",** and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof"

5) In claim 71, line 10, after "buprenorphine or" **INSERT** "physiologically acceptable"

6) In claim 71, line 12, after "2 hours" **INSERT** ", and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof"

7) In claim 72, line 7, after "to be treated" **INSERT** ", and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof"

8) In claim 74, line 7, after "to be treated" **INSERT** ", and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof"

DETAILED ACTION

Application Priority

This application is a national entry of PCT/GB03/01183, and claims priority to foreign applications (0206448.3, 0225040.5, 0225041.3, 0225042.1) filed in the United Kingdom on 3/19/2002 and 10/28/2002.

REASONS FOR ALLOWANCE

The rejection of claims 1, 13, 38, 39, 41 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 8, and 12 of U.S. Patent No. 6,387,917 in view of Eriksen et al. and Watts et al. and Ni et al, rejection of claims 1-10, 12-15, 38-39, 41, 48-52, 67-71 under 35 U.S.C. 103(a) as being unpatentable over Eriksen et al. in view of Watts et al. and Ni et al., claim 11 under 35 U.S.C. 103(a) as being unpatentable over Eriksen et al. (in view of Watts et al. and further in view of Reich et al. and Nairn and Remington is withdrawn due to Applicants' arguments and amending claims to a limitation that reads on wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof". The double patenting rejection of claims 1-15, 38, 39, 41, 48-52, 67-71 as being unpatentable over claims 1-56 of co-pending application No. 11/798,384 is withdrawn due to Applicants' filing a Terminal Disclaimer on 7/16/2009. Claims 1-15, 38, 39, 41, 70-72, 74-77, 79 are allowable and are renumbered as 1-26.

The following is an examiner's statement of reasons for allowance:

Claims 1, 70, 71, 72, 74 and 79 are drawn to an aqueous solution suitable for intranasal administration, which comprises buprenorphine or a physiologically acceptable salt or ester thereof and pectin having a degree of esterification of less than 50%; which solution has a pH of from 3 to 4.2, is substantially free from divalent metal ions and gels on the nasal mucosa, and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof, claims 14 and 15 are directed to a process for the preparation of an aqueous solution, claim 41 is towards a method of inducing analgesia comprising administering an aqueous solution of claim 1. The closest prior art of record is Eriksen et al. and Watts et al. Eriksen teaches an aqueous solution comprising buprenorphine for intranasal administration. Eriksen do not reach solutions comprising pectin or solutions with a pH of 3-4.2 comprising buprenorphine and pectin. Watts et al. teach solutions comprising analgesic drugs such as nicotine, fentanyl and pectin that has a low degree of esterification. The reference states that for local delivery of drugs it is important to retain the drug at its site of action, namely nasal and in such cases the formulation should not enhance the absorprion of the drug and further teaches in example 3 that the pectins with low DE do not enhance the nasal uptake of a model polar drug. Watts reference does not teach or suggest show in any examples the enhanced absorption of the drug or an increase in bioavailability upon addition of low DE pectin. Also, buprenorphine is a weakly basic compound having a pKa of about 8.3, which is almost identical to that of nicotine, which has a pKa of about 8.5 and formulations comprising nicotine together with pectins having low degree of esterification are exemplified in Watts (page 25,

Example 2), which refers to the compound as a weak base and t was found by Watts that no gelation occurred when nicotine was used. Accordingly, it is not obvious from Watts that gellation occurred when pectin was added to any type of drug. Also prior art teachings show sublingual buprenorphine has a bioavailability of 56% and intranasal buprenorphine in dextrose solution has a bioavailability of 48%. There is no anticipation or motivation of formulating an aqueous solution of buprenorphine with low DE pectin at a pH from 3 to 4.2, wherein the solution provides a bioavailability of 80%or more of the buprenorphine and physiologically acceptable salt thereof from the teaching or suggestion from prior art.

The claims are allowable over the closest art of record because they do not teach, disclose nor make obvious the claimed aqueous solution suitable for intranasal administration, which comprises buprenorphine or a physiologically acceptable salt or ester thereof and pectin having a degree of esterification of less than 50%; which solution has a pH of from 3 to 4.2, is substantially free from divalent metal ions and gels on the nasal mucosa, and wherein said solution provides a bioavailability of 80% or more of the buprenorphine or physiologically acceptable salt or ester thereof, the process for the preparation of such aqueous solution, and a method of inducing analgesia comprising administering such aqueous solution of claim 1.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617